December 18, 2003

James E. McLaughlin, Ph.D.
Toxicology Program Manager
Rohm and Haas Company
727 Norristown Road
P.O. Box 0904
Spring House, PA 19477-0904

Dear Dr. McLaughlin:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Primene 81-R amines posted on the ChemRTK HPV Challenge Program Web site on August 19, 2003. I commend Rohm and Haas Company for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Rohm and Haas Company advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Primene™ 81R Amines

Summary of EPA Comments

The sponsor, Rohm and Haas Company, submitted a test plan and robust summaries to EPA for Primene™ 81R amines (C_{12}-C_{14} t-alkyl amines; CAS No. 68955-53-3) dated April 25, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on August 19, 2003.

EPA. has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The data provided by the submitter for these endpoints are adequate for the purposes of the HPV Challenge Program.

2. Environmental Fate. The submitter needs to provide hydrolysis data and needs to provide the input values used in the fugacity model.

3. Health Effects. The submitted data are adequate to address all health effects endpoints for the purposes of the HPV Challenge Program. The submitter needs to address a few deficiencies in the robust summaries.

4. Ecological Effects. The submitted acute toxicity data for fish, invertebrates and algae and fish chronic toxicity data are adequate for the purposes of the HPV Challenge Program.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on The Primene™ 81r Amines Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The submitted data are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The submitted data for photodegradation and biodegradation are adequate for the purposes of the HPV Challenge Program.

Stability in water. The submitter needs to provide hydrolysis data following OECD guidelines.

Fugacity. The submitter needs to provide the input values used for the calculation of its fugacity model.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Submitted data are adequate to address all health effects endpoints for the purposes of the HPV Challenge Program. The submitter needs to address a few deficiencies in the robust summaries. EPA has the following comments on the submitted data:

Developmental Toxicity. The submitted dermal-exposure teratogenicity study is insufficient to represent the developmental toxicity endpoint because of uncertainty as to systemic penetration of the test material; however, the submitted one-generation reproductive toxicity assay adequately addresses the endpoint.

Ecological Effects (fish, invertebrates, and algae).

All appropriate SIDS-level endpoints have been addressed for the purposes of the HPV Challenge Program.

Specific Comments on the Robust Summaries

Health Effects

Acute Toxicity. A robust summary for an acute oral toxicity study (Ref. 24) omitted the method for calculating the $LD_{50.}$ In addition, there is a discrepancy in LD_{50} values given in the Values field (>500 mg/kg) and those given in the Conclusions field (1177 mg/kg for males and 612 mg/kg for females).

A summary for an acute oral toxicity study (reference 19) incorrectly flagged the study as a critical study, although it assigned Klimisch code 4 (critical studies can only receive a code of 1 or 2).

Repeated-Dose Toxicity. The submitter needs to provide the magnitude of the observed reductions in body weight gain in the robust summary for a 4-week inhalation study in rats.

Genetic Toxicity. A robust summary for a positive mutagenicity assay (Ref. 8) omitted information on the cytotoxic concentrations and the concentration at which positive results were observed in TA1535 without metabolic activation.

The robust summary for a negative micronucleus assay in rats lacks information on the number of erythrocytes examined per dose.

Reproductive Toxicity. The missing information from the one-generation reproductive toxicity study summary includes exact dosing regimen and the magnitude of body weight reduction in parents and pups.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.